Visceral Adiposity Index is not Superior over Anthropometric Parameters with regards to Inflammation in Healthy Adolescent Girls

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Objective: Better than simple anthropometric parameters, the visceral adiposity index (VAI) has recently been proposed as a predictor of cardiometabolic risk in adults. However, there are conflicting results on the associations of these parameters in children and adolescents. Therefore, we aimed to estimate this potential relationship between VAI, anthropometric parameters (i.e., body mass index [BMI], waist circumference [WC], and waist-to-height ratio [WHtR], respectively), and inflammation as measured by high-sensitivity C-reactive protein (hs-CRP) levels in a cohort of adolescent girls.

Methods: A total of 90 adolescent girls from 16 to 19 years old were included in cross-sectional study. Anthropometric and biochemical parameters (glucose, lipid parameters, and hsCRP) were measured. The VAI, derived from anthropometric and lipid parameters, calculated {[WC/36.58 + (1.89 × BMI)] × (triglycerides/0.81) × (1.52/ HDL-cholesterol)} was calculated.

Results: A comparison of the receiver operating characteristic (ROC) curves showed that all the curves for the anthropometric parameters (e.g., BMI, WC, WHtR) had excellent discriminatory capability with regard to inflammation level status (low vs. high level) and significantly larger areas under the curve (AUC = 0.885, AUC = 0.863, AUC = 0.860, respectively; P<0.001) than the ROC curve for VAI did (AUC = 0.686; P = 0.021).

Conclusion: Visceral adiposity index is not superior over anthropometric parameters in relation to inflammation as measured by high sensitivity C-reactive protein in adolescent girls. [*P R Health Sci J 2018;37:195-199*]

Key words: Adolescents, Inflammation, Obesity, Visceral adiposity index

It is well established that obesity is characterized by low-grade inflammation (1). Adipocytes and macrophages from enlarged adipose tissue are significant sources of pro-inflammatory cytokines (e.g., high-sensitivity C-reactive protein [hs-CRP], interleukin 6 [IL-6], tumor necrosis factor alpha [TNF-a]) which impair insulin signaling, thus resulting in variety of obesity-related comorbidities (2).

Even though cardiovascular disease (CVD) is rarely manifested before adulthood, cardiovascular risk often begins in childhood and adolescence, especially in relation to obesity (1). Higher levels of hs-CRP are directly associated with many cardiometabolic risk factors (3, 4), thus emphasising the inflammation as underlying feature of cardiometabolic processes, as well as the important link between obesity and CVD (3).

The visceral adiposity index (VAI) is proposed to be a simple and low-cost tool for the evaluation of adipose tissue dysfunction and its associated cardiometabolic risk in adult population (5). However, despite the fact that a large number of studies in adult population indicate VAI as more reliable marker of cardiometabolic risk than body mass index (BMI) and waist circumference (WC) (5–8), there are others that reject its superiority over simple anthropometric indices (9–13).

To our knowledge, only 1 study has investigated the reliability of the VAI as a marker of early cardiometabolic risk in children and adolescents (9). Since the data in adolescent

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population are scarce, we aimed to estimate the potential relationship between VAI, anthropometric parameters (i.e., BMI, WC, waist to height ratio [WHtR], respectively), and inflammation as measured by hs-CRP in a cohort of adolescent girls from 16 to 19 years old.

Materials and Methods

Study population

This study derived from a previous work aiming to assess cardiovascular risk in adolescent girls (14).

A total of 90 Caucasian girls (of them 45 obese) between the ages of 16 and 19 were included in this cross-sectional study. All volunteers were selected from 2 high schools in Podgorica, Montenegro, and were recruited in the Primary Health Care Center for examination, in a period from December 2012 to March 2013. The methods and assays used to include examinees and to exclude disorders in examined adolescent girls have been described in detail elsewhere (14).

The study protocol was approved by the Institutional Review Board (IRB) of Primary Health Care Center in Podgorica, Montenegro and the research was carried out in compliance with the Declaration of Helsinki.

Biochemical parameters

Biochemical parameters were measured as previously described (14). The blood samples were taken between 7 and 9 a.m., after 12 to 14 hours of an overnight fast. Serum levels of fasting glucose, total cholesterol (TC), high density lipoprotein cholesterol (HDL-c), low density lipoprotein cholesterol (LDL-c) and triglycerides (TG) were measured using standardized enzymatic procedures, spectrophotometrically (Roche Cobas 400, Mannheim, Germany). Levels of hs-CRP were determined using a nephelometric assay (Behring Nephelometer Analyzer, Marburg, Germany).

Anthropometric measurements

Anthropometric measurements: body height (cm), body weight (kg) and WC (cm) were obtained, and BMI was calculated, as described previously (14). Waist to height ratio (WHtR) was calculated as WC (cm) divided by height (cm). VAI was calculated using formula:

$\{[WC/36.58 + (1.89 \times BMI)] \times (TG/0.81) \times (1.52/HDL\text{-}c)\}$, as described elsewhere (13, 15).

Statistical analysis

Data are presented as mean ± standard deviation, median (interquartile range), or counts and percentages. In order to examine the association of increased inflammation level (as measured by hs-CRP level) with obesity status, anthropometric indices and VAI, so as with metabolic risk factors, we divided patients according to tertile values of hs-CRP. Differences between groups were evaluated with a Student's t test for normally, Mann-Whitney test for non-normally distributed parameters, or 1-way ANOVA, and Kruskal–Wallis non-parametric analysis of variance where appropriate. The differences between categorical data were evaluated with Chi-squared test. The possible relationship between serum hs-CRP and clinical and biochemical characteristics in the group of obese girls was tested with Spearman's (ρ) correlation coefficient. Receiver Operating Characteristic (ROC) curve analysis was used with the purpose of testing discriminatory potential of anthropometric parameters as well as VAI, with hsCRP as dependent variable. The area under the ROC curve (AUC) suggested the excellent discriminatory capability (AUC>0.800, according to Hosmer and Lemeshow rules) towards inflammation status level (low vs. higher hs-CRP level) (16). In all analyses P value of < 0.05 was considered as statistically significant. Statistical calculations were performed using SPSS statistical package (version 15.0 for Windows, SPSS, Chicago, IL, USA).

Results

Table 1 shows the association of increased inflammation level (as measured by hs-CRP level) with obesity status, anthropometric indices and VAI, so as with metabolic risk factors.

Significantly higher number of obese subjects, as well as significantly lower number of normal weight counterparts were in the group with the highest hs-CRP values ($\chi 2 = 29.41$,

Table 1. General characteristics of adolescent girls divided into hs-CRP tertile values subgroups

	Hs-CRP tertile values			
	I tertile (n = 20) ≤0.33 mg/L	II tertile (n = 32) 0.34–0.66 mg/L	III tertile (n = 38) ≥0.67 mg/L	P
Age (years)	17.8±1.11	18.0±1.12	17.8±1.13	0.841
BMI (kg/m²)	21.2±2.15^{aaa,bbb}	24.2±3.31^{aaa}	27.6±4.51	<0.001
BMI z-score	-0.08±0.74^{aaa,bb}	0.67±3.30^{aa}	1.22±0.81	<0.001
WC (cm)	78 (67–89)^{aaa,bbb}	80 (72–102)^{aaa}	95 (84–103)	<0.001
WHtR	0.46 (0.42–0.49)^{aaa,b}	0.47 (0.46–0.52)^{aaa}	0.56 (0.50–0.59)	<0.001
VAI	0.92 (0.59–1.26)^{a}	1.12 (0.62–2.14)	1.26 (0.90–1.92)	0.049
Glucose(mmol/L)	4.96±0.29^{a}	5.07±0.35	5.26±0.49	0.019
TC (mmol/L)	4.12±0.59	4.27±0.65	4.26±0.68	0.681
HDL-c (mmol/L)	1.41 (1.27–1.83)^{a}	1.36 (1.23–1.73)	1.25 (1.13–1.52)	0.057
LDL-c (mmol/L)	2.34±0.55	2.37±0.56	2.48±0.52	0.568
TG (mmol/L)#	0.69 (0.54–0.92)	0.77 (0.61–1.12)	0.84 (0.69–1.17)	0.175
Obese/normal weight, n (%)	0/20 0/44	16/16 36/36	29/9 64/20	$\chi^2 = 29.41$ P<0.001

aaap<0.001, aap<0.01, ap<0.05 vs. third hs-CRP tertile; bbbp<0.001, bbp<0.01, bp<0.05 vs. second hs-CRP tertile
Data are presented as mean ± standard deviation or #- data with non-Gaussian distribution are shown as median values (interquartile range), or counts and percentages;*P value from 1-way ANOVA or Kruskal–Wallis non-parametric analysis of variance, followed by non-parametric Mann–Whitney U test, where appropriate; BMI: body mass index; WC: waist circumference; WHtR: waist-to-height ratio; VAI: visceral adiposity index; TC: total cholesterol; HDL-c: high density lipoprotein cholesterol; LDL-c: low density lipoprotein cholesterol; TG: triglycerides; hs-CRP: high sensitivity C-reactive protein

P<0.001). Moreover, with increasing tertiles of serum hs-CRP levels, significant increase in anthropometric parameters (i.e., BMI, BMI z-score, WC, WHtR), (P<0.001, respectively), VAI (P = 0.049) and fasting glucose (P = 0.019) were found. However, there was no difference in lipid parameters across hs-CRP tertile values.

Table 2. Spearman's non-parametric correlation between serum hs-CRP concentration and clinical variables in the group of obese adolescent girls (n = 45)

Variable	Rho (ρ)	P
Age (years)	0.020	0.893
BMI (kg/m²)	0.567	<0.001
BMI z-score	0.596	<0.001
WC (cm)	0.684	<0.001
WHtR	0.629	<0.001
VAI	0.322	0.033
Glucose (mmol/L)	0.413	0.006
TC (mmol/L)	-0.058	0.702
LDL-c (mmol/L)	0.071	0.639
HDL-c (mmol/L)	-0.252	0.095
TG (mmol/L)	0.310	0.040

BMI: body mass index; WC: waist circumference; WHtR: waist-to-height ratio; VAI: visceral adiposity index; TC: total cholesterol; HDL-c: high density lipoprotein cholesterol; LDL-c: low density lipoprotein cholesterol; TG: triglycerides; hs-CRP: high sensitivity C-reactive protein

Table 2 shows the relationship between serum hs-CRP and clinical and biochemical characteristics in the group of obese girls (n = 45).

Serum hs-CRP correlated positively with all anthropometric measures (i.e., BMI, BMI z-score, WC, WHtR), (ρ = 0.567, ρ = 0.596, ρ = 0.684, ρ = 0.629; P<0.001, respectively), VAI (ρ = 0.322, P = 0.033), fasting glucose (ρ = 0.413, P = 0.006), and TG (ρ = 0.310, P = 0.040) in obese adolescent girls.

Figure 1 shows ROC curve graph and Table 3 shows the most important ROC parameters: area under the curve (AUC) with 95% confidence interval (CI) of selected parameters. Table 3. also shows sensitivities, specificities and cut-off values for selected parameters.

ROC analysis showed that all curves for anthropometric parameters (i.e., BMI, BMI z-score, WC, WHtR) have comparable and excellent discriminatory capability (AUC>0.800) towards inflammation status level (low vs. higher hs-CRP level).

Furthermore, the same analysis showed that all curves for anthropometric parameters (e.g., BMI, BMI z-score, WC, WHtR) had significantly larger area under the curve (AUC = 0.885, AUC = 0.880, AUC = 0.863, AUC = 0.860, P<0.001, respectively), than ROC curve for VAI (AUC = 0.686, P = 0.021). The best clinical accuracy, according to this analysis showed BMI for the cut-off value of 24.4 kg/m2, which means that subjects with BMI larger than 24.4 kg/m2 are more likely to have increased inflammation.

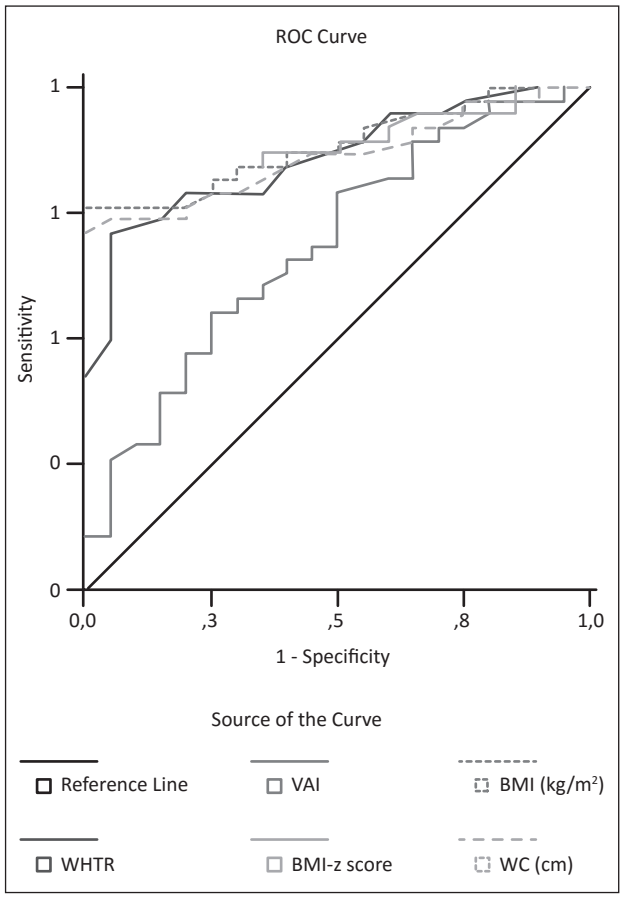

Figure 1. ROC curves of selected parameters' discriminatory ability regarding hs-CRP level (low vs. higher level)

Discussion

In the current study we evaluated the relationship between VAI, anthropometric parameters (i.e., BMI, WC, WHtR, respectively), and inflammation, as measured by hs-CRP in healthy adolescent girls. Our results show that VAI is not superior over anthropometric parameters in relation to inflammation in this cohort. The cross-sectional study, conducted by Al-Daghri et al. (9) that included a total of 619 apparently healthy Saudi

Table 3. Area under the curve, 95% confidence interval and standard error for the parameters of selected parameters' discriminatory ability regarding hs-CRP level (low vs. higher level); pairwise comparison of the areas under ROC curves (AUCs) for all parameters

Parameter	AUC	95% CI	SE	Sensitivity (%)	Specificity (%)	Cut-off value	P
BMI	0.885	0.802-0.968	0.043	76.3	95.0	24.4	<0.001
BMI z-score	0.880	0.794-0.966	0.044	76.3	95.0	0.845	<0.001
WC	0.863	0.771-0.955	0.047	88.0	73.7	95.0	<0.001
WHtR	0.860	0.766-0.953	0.048	71.1	95.0	0.515	<0.001
VAI	0.686	0.543-0.830	0.073	55.3	75.0	1.16	0.021

AUC: area under the ROC curve; CI: confidence interval; SE: standard error; BMI: body mass index; WC: waist circumference; WHtR: waist-to-height ratio; VAI: visceral adiposity index; hs-CRP: high sensitivity C-reactive protein

boys and girls aged 4 to 17 years, also reported inferiority for VAI relative to BMI and WC in relation to cardiometabolic parameters. These findings may implicate that overall adiposity in children as assessed by BMI can better explain increased cardiometabolic risk and subclinical inflammation compared with visceral obesity as reflected by the VAI (9).

Opposite to Al-Daghri et al. (9) who did not report association of VAI with inflammation level, we reported increase in VAI across hs-CRP tertile groups. However, ROC analysis showed that ROC curves for all examined anthropometric parameters had better discriminatory capability towards inflammation status level than for VAI.

In line with this, we previously reported that VAI is not superior over anthropometric indices for type 2 diabetes mellitus prediction in adult population (13).

On the contrary, the first study on the VAI (6), in a population of almost 1,500 Caucasian primary care patients, showed strong independent association with both cardiovascular and cerebrovascular events. In addition, ROC analysis displayed greater sensitivity and specificity of VAI, compared to WC and BMI with regard to cardio- and cerebrovascular events. In the other study, VAI better correlated with hs-CRP than anthropometric measures (17).

However, our results are opposite, showing that BMI, WC and WHtR displayed greater subjects' categorization according to their inflammation status, than VAI (Table 3, Figure 1). The best clinical accuracy, according to this analysis showed BMI for the cut-off value of 24.4 kg/m2, which means that subjects with BMI larger than 24.4 kg/m2 are more likely to have increased inflammation.

Of note, our current study encompassed 50% of overweight/obese adolescent girls although epidemiological data in Montenegro from 2015 reported that the prevalence of childhood overweight and obesity was 22.9% and 5.3%, respectively (18). Nevertheless, we previously reported that BMI and WC correlated with cardiometabolic parameters even in normal weight and overweight adolescent population (19), thus considering them as reliable parameters in relation to cardiometabolic risk.

In line with this, in a large study that encompassed more than 4,000 children of 6 years age, Toemen at al. (20) showed that all fat mass measures were associated with increased CRP, even after adjustment for confounding factors, suggesting that higher general and abdominal fat mass may lead to increased CRP levels even at younger age.

However, there are conflicting results in literature on the strength of the relationship between anthropometric indices and cardiometabolic risk factors in children and adolescents. While some studies reported stronger correlation between abdominal obesity indices (e.g., WC, WHtR) compared with overall obesity (e.g., BMI) (21–23), some others showed no difference between them in relation to cardiometabolic risk estimates (24–26).

In addition, in a recent cross-sectional analysis with 529 Portuguese adolescents the highest areas under the ROC curves were presented by BMI and WHtR for CRP, only in girls and by WC for CRP only in boys (27).

The possible discrepancies in results may be due to the lack of WC cutoff values in children validated for identifying those with the greatest cardiometabolic risk (28). Moreover, WC reference values may differ from one country to another, considering the fact that genetic and environmental factors may have an impact on the variations in the WC phenotype. Above this, a standardized technique for measuring WC in children lacks which may lead to discrepancies when comparing results between studies (28).

It should be emphasized that the current study has some limitations. Firstly, the small number of participants is a limitation for a study dealing with the estimation of reliability of anthropometric indices in relation to inflammation. Furthermore, since we included in our study only girls, and since the causal relationship between anthropometric indices and hs-CRP could not be established, prospective studies including both genders are needed to clarify the potential superiority of VAI over simple anthropometric indices in obesity-related disorders.

Amato et al. pointed out the limitation for application of the VAI in non-Caucasian populations and in patients aged less than 16 years (5). Since our cohort included only Caucasian girls older than 16 years, who were healthy and not receiving any medicament therapy which might affect metabolic parameters and hs-CRP level (4), and since we reported results opposite to Amato et al. (5) more research is needed when interpreting utility of VAI in relation to inflammation in adolescent population.

Nevertheless, our study included a cohort of adolescent girls to whom simple and low-cost anthropometric measures were obtained and all of those parameters showed an excellent diagnostic accuracy toward inflammation status levels (as measured by hs-CRP). Therefore, anthropometric indices should be routinely measured, especially in overweight/obese adolescents as significant indicators of high cardiometabolic risk.

Resumen

Objetivo: El índice de adiposidad visceral (IAV) ha sido propuesto recientemente como predictor de riesgo cardiometabólico, más que simple parámetro antropométrico en los adultos. No obstante, los resultados de estos predictores en niños y adolescentes son contradictorios. El objetivo de este estudio fue analizar la asociación potencial entre IAV, los parámetros antropométricos (i.e., el índice de masa corporal (IMC), la circunferencia de cintura (CC), la razón cintura-estatura (RCE) así como la inflamación medida por la proteína C-reactiva de alta sensibilidad (PCR) en un cohorte en niñas adolescentes. Métodos: En este estudio transversal se incluyeron un total de 90 niñas adolescents de 16 a 19 años. Se obtuvieron marcadores antropométricos y bioquímicos (glucosa, parámetros lipídicos y PCR). IAV fue evaluado,

derivado de los parámetros antropométricos y lípidos séricos {[CC/36.58 + (1.89 × IMC)] × (Triglicéridos/0.81) × (1.52/HDL-colesterol)}. Resultados: Curva ROC (El receptor de funcionamiento característico) usada para el análisis mostró que todas las curvas antropométricas (IMC, CC, RCE) tenían excelente capacidad discriminatoria hacia el estado del nivel de la inflamación (nivel bajo vs. nivel alto) y área significativamente mayor bajo la curva (AUC=0.885, AUC=0.863, AUC=0.860, P<0.001, respectivamente), que la curva ROC para IAV (AUC=0.686, P=0.021). Conclusión: El índice de adiposidad visceral no es superior al parámetro antropométrico en cuanto a la inflamación medida por la proteína C-reactiva de alta sensibilidad de las niñas adolescentes.

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